QIAprep Spin Miniprep kit (Qiagen), circularized by ligation in 50 µl reaction and transformed by electroporation of 1.5 µl of ligation reaction into the DH10B (Gibco/BRL) strain of *E. coli*. Colonies carrying the P-element were selected by plating transformed bacteria on media with Kanamycin. DNA was isolated from positive colonies and the approximate size of the insert (flanking genomic DNA) determined by AvaI restriction enzyme digestion. Inserts of sufficient size were sequenced by automated sequencing and the results were compared with known DNA or protein sequences in the database by Berkeley Drosophila Genome Project (BDGP) BLAST server (BLASTN) and The Baylor College of Medicine Search Launcher (BLASTP+BEAUTY). Protein alignments were performed by MacVector PPC 6.0.1 application software. Program parameters for *Drosophila* dTPR2 and human TPR2 were Clustal W(1.4), Pairwise alignment mode: slow: Open Gap penalty 10.0: Extend gap penalty 0.1; similarity matrix blosum. For *Drosophila* dMLF and human MLF the program parameters were Clustal W(1.4), Pairwise alignment mode: slow: Open Gap penalty 1.0: Extend gap penalty 0.1; similarity matrix blosum. EST search parameters were BLASTN 2.0a19MP.--

In the claims:

Please cancel claims 4, 8 and 27.

Please amend claims 1, 2, 5, 6, 9-13, 25, 26, 28-46 and 50 as follows:

1. (Amended) A method of screening for genes that modulate polyglutamine toxicity comprising:

(a) providing a first Drosophila expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity in the Drosophila;

(b) breeding the first Drosophila to a second Drosophila, wherein the second Drosophila has a marker sequence inserted into its germline, wherein the marker sequence comprises 1) an inducible upstream activating sequence, 2) a minimal promoter sequence and 3) 5′ and 3′ transposable elements;

(c) producing progeny from the breeding of the first Drosophila with the second Drosophila;

(d) screening the progeny for increased or decreased polyglutamine toxicity relative to the first Drosophila thereby identifying a progeny having increased or decreased polyglutamine toxicity; and

(e) identifying one or more genes operationally-associated with the marker sequence, or having an insertion of the marker sequence, that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity.

2. (Amended) The method of claim 1, further comprising identifying a mammalian homologue of the gene of claim 1.

5. (Amended) The method of claim 1, wherein the Drosophila is Drosophila melanogaster.

6. (Amended) The method of claim 1, wherein the transposable element comprises a P transposable element.

9. (Amended) The method of claim 1, wherein the inducible upstream activating sequence increases or decreases expression of one or more operationally-associated gene(s).

Sub B2

10. (Amended) The method of claim 1, wherein the second Drosophila is selected from a group of two or more animals having markers inserted into different locations of its genomic DNA.

11. (Amended) The method of claim 10, wherein the second Drosophila is selected from a group of 10 to 100, 100 to 500, or 500 or more of the animals.

12. (Amended) The method of claim 1, wherein the second Drosophila is selected from a library of animals having markers inserted at random locations of their genomic DNA.

13. (Amended) The method of claim 12, wherein the library of Drosophila is generated by random P element insertion.

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25. (Amended) A progeny Drosophila produced by the method of claim 1.

26. (Amended) A transgenic Drosophila comprising a transgene containing a plurality of CAG's and at least one CAA sequence encoding a polyglutamine repeat sequence.

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28. (Amended) The Drosophila of claim 26, wherein the Drosophila is Drosophila melanogaster.

Sub B4

29. (Amended) The Drosophila of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 1:1 and 2:1.

30. (Amended) The Drosophila of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 2:1 and 5:1.

31. (Amended) The Drosophila of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 5:1 and 10:1.

32. (Amended) The Drosophila of claim 26, wherein the number of CAG's to CAA's is in ratio of between about 10:1 and 50:1.

33. (Amended) The Drosophila of claim 26, wherein expression of the polyglutamine sequence is conferred by a constitutive, regulatable or tissue specific expression control element.

34. (Amended) The Drosophila of claim 33, wherein the tissue specific expression control element confers neural, retinal, muscle or mesoderm cell expression.

35. (Amended) The Drosophila of claim 33, wherein the tissue specific expression control element comprises an Appl or rhodopsin 1 promoter or GLASS transcription factor element.

36. (Amended) The Drosophila of claim 26, wherein the polyglutamine sequence is between about 30 and 50 amino acids in length.

37. (Amended) The Drosophila of claim 26, wherein the polyglutamine sequence is between about 50 and 100 amino acids in length.

38. (Amended) The Drosophila of claim 26, wherein the polyglutamine sequence is between about 100 and 200 amino acids in length.

39. (Amended) The Drosophila of claim 26, wherein the polyglutamine sequence is between about 50 and 200 amino acids in length.

40. (Amended) The Drosophila of claim 26, wherein the polyglutamine sequence further comprises a tag.

41. (Amended) The Drosophila of claim 26, wherein polyglutamine toxicity is produced in one or more tissue or organs of the animal.

42. (Amended) The Drosophila of claim 26, wherein the animal further comprises a marker sequence inserted into its genomic DNA, wherein the marker is located adjacent to a gene or inserted into a gene whose expression or activity increases or decreases polyglutamine toxicity in the animal, and wherein the marker sequence comprises an inducible upstream activating sequence, a minimal promoter sequence and 5′ and 3′ transposon elements containing terminal inverted repeats.

43. (Amended) The Drosophila of claim 42, wherein the marker sequence is near or inserted into a gene containing a J domain.

44. (Amended) The Drosophila of claim 43, wherein the gene is HDJ1.

B4 cancel

45. (Amended) The Drosophila of claim 43, wherein the gene is TPR2.

Q9 cancel

46. (Amended) The Drosophila of claim 43, wherein the marker sequence is near an MLF gene.

Q10 B5

50. (Amended) A method of producing a transgenic Drosophila characterized by polyglutamine toxicity comprising:

(a) transforming a Drosophila embryo or fertilized egg with a transgene comprising a plurality of CAA and CAG sequences encoding a polyglutamine sequence having a length sufficient to produce polyglutamine toxicity in the Drosophila produced from the embryo or fertilized egg; and

(b) selecting a[n animal] Drosophila that exhibits polyglutamine toxicity in one or more cells or tissues.

Informal Matters

The Office Action alleges that the Declaration is not legible. Applicants will provide a legible Declaration.